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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,108	12/10/2004	Lai-Xi Wang	4115-186	3314
24239 7590 09/27/2007 MOORE & VAN ALLEN PLLC P.O. BOX 13706 Research Triangle Park, NC 27709			EXAMINER LEWIS, PATRICK T	
			ART UNIT 1623	PAPER NUMBER
			MAIL DATE 09/27/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/518,108

Applicant(s)

WANG ET AL.

Examiner

Patrick T. Lewis

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 September 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4,9-11,15,16,19,25,26,28,29 and 37 is/are pending in the application.
- 4a) Of the above claim(s) 11,15,19,25,26,28,29 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4,9,10 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on December 10, 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of Group I, claims 1-4, 9-10 and 16, in the reply filed on September 13, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 11, 15, 19, 25-26, 28-29 and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 13, 2007.

### ***Claim Objections***

3. Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 limits the core to a monosaccharide.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

Art Unit: 1623

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4, 9-10 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a maleimide cluster comprising one core carbohydrate, does not reasonably provide enablement for a maleimide cluster comprising more than one core carbohydrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

These factors include, but are not limited to:

1. the breadth of the claims;
2. the nature of the invention;
3. the state of the prior art;
4. the level of one of ordinary skill in the art;
5. the level of predictability in the art;
6. the amount of direction provided by the inventor;
7. the existence of working examples; and
8. the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 1-4, 9-10 and 16 are drawn to a maleimide cluster comprising at least one core carbohydrate molecule wherein at least two or more maleimides are attached to the core and optionally comprising a protein.

Undue experimentation is required to determine the synthetic protocol for obtaining a maleimide cluster comprising more than one carbohydrate molecule. There has not been provided adequate guidance in the written description for accomplishing such, as only one maleimide clusters containing a single carbohydrate core are described in the specification. Without guidance as to chemical structure and method for obtaining maleimide clusters containing more than one core carbohydrate, undue experimentation would be required. Applicant should note that oligosaccharides, polysaccharides, cyclic oligosaccharides and fused saccharides are viewed as a single core.

It is noted that while there are some working examples showing maleimide clusters containing a single carbohydrate core, it is not seen as sufficient to support the invention of the claims. The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to enable making maleimide clusters containing more than one carbohydrate core. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make

Art Unit: 1623

and use the invention as of its filing date, *In re Glass*, 181 USPQ 31; 492 F.2d 1228 (CCPA 1974). A broad claim requires a correlatively broad and sufficient disclosure to support it. Examples and description should be of sufficient scope as to justify the scope of the claims. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1-4 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brask et al. Journal of peptide Science (2000), Vol. 6, pages 290-299 (Brask) and Nefzi et al. Tetrahedron Letters (1995), Vol. 36, pages 229-230 (Nefzi) in combination.

Claims 1-4, 9-10 and 16 are drawn to a maleimide cluster comprising at least one core carbohydrate molecule wherein at least two or more maleimides are attached to the core and optionally comprising a protein.

Brask teaches multifunctional, topological template molecules such as linear and cyclic peptides have been used for the attachment of peptide strands to form novel protein models (Abstract). The concept of carbohydrates as templates for de novo design of potential protein models has been previously described and these novel chimeric compounds were termed carbopeptides. (page 290) To bypass the problematic folding step of linear polypeptides, Mutter and coworkers have suggested a template-assembled synthetic proteins (TASP) concept which relies on a multifunctional topological scaffold or template, which enhances the spatial accommodation of the peptides. Carbohydrates are promising candidates for templates for the display of functional groups due to their inherent multifunctionality, the relative rigidity of ring

forms, ease of regioselective chemical manipulations, and access to stereoisomers of mono- and disaccharides (page 291). The preparation of carbopeptides by oxime ligation is shown in Figures 2-5. In a model study, 2,4-dimethoxybenzaldehyde was coupled to methyl 2,3,4,6-tetra-O-Aca- $\alpha$ -D-Galp (7) at room temperature (page 296).

Brask differs from the instant invention in that Brask does not teach a TASP containing maleimide functions; however, it would have been obvious to one of ordinary skill in the art at the time of the invention to do so in view of the teachings of Nefzi.

Nefzi teaches a method of chemoselective ligation for TASP synthesis using the maleimide function, which is known to react rapidly and rather selectively with thiols (page 229). This should allow for the condensation of peptides containing a thiol group to template molecules containing the maleimide function. Applicant's attention is directed to Scheme 1 wherein Nefzi shows a maleimide function covalently attached to a template which is then reacted with a thiol-containing peptide.

It would have been obvious to one of ordinary skill in the art at the time of the invention to attach peptides to a maleimide function covalently linked to a template. One would have been motivated to incorporate a maleimide function because they are known to react rapidly and rather selectively with thiols. It would have also been obvious to one of ordinary skill in the art to select a monosaccharide as the template. As taught by Brask, carbohydrates are promising candidates for templates for the display of functional groups due to their inherent multifunctionality, the relative rigidity of ring forms, ease of regioselective chemical manipulations, and access to stereoisomers of mono- and disaccharides.



### ***Conclusion***

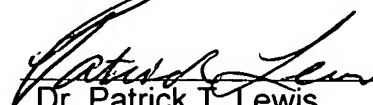
10. Claims 1-4, 9-11, 15-16, 19, 25-26, 28-29 and 37 are pending. Claims 1-4, 9-10 and 16 are rejected. Claims 11, 15, 19, 25-26, 28-29 and 37 are withdrawn from further consideration as being drawn to a nonelected invention. No claims are allowed.

### ***Contacts***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Dr. Patrick T. Lewis  
Primary Examiner  
Art Unit 1623

ptl